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EXAMINER	
PATTEN, PATRICIA A	

ART UNIT	PAPER NUMBER
1651	

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13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/665,036	Ilic et al.
Examiner	**Art Unit**
Patricia Patten	1651

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *Jan 9, 2002* .

2a) [ ] This action is **FINAL.** 2b) [X] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *1-39* is/are pending in the application.

4a) Of the above, claim(s) *1-4 and 11-18* is/are withdrawn from consideration.

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *5-10 and 19-39* is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are objected to by the Examiner.

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____ .
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) [X] Notice of References Cited (PTO-892)
16) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) [ ] Information Disclosure Statement(s) (PTO-1449) Paper No(s)
18) [ ] Interview Summary (PTO-413) Paper No(s).
19) [ ] Notice of Informal Patent Application (PTO-152)
20) [ ] Other:

DETAILED ACTION

Claims 1-33 are pending in the application.

Claims 1-4 and 11-18 have been withdrawn from consideration as being drawn to a non-elected invention in Paper No. 6.

Claims 5-10 and 19-39 have been presented for examination on the merits.

Applicants arguments presented 1/9/02 were fully considered. It was deemed that in fact, the references disclosed pulverizing the seeds prior to defatting, thus, the epidermal layers under the wax layer was not substantially intact after extraction. Therefore, the rejection under the previous references fall. However, upon studying the extraction protocols disclosed in the Instant Specification, it is deemed that new rejections are in order.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5, 36 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 recites 'the epidermis.' This phrase lacks antecedent basis in the claim.

Claim 36 recites 'brief period.' This term is indefinite in that the meets and bounds of the phrase are not clearly delineated. The term 'brief' is a subjective term which may have respective meanings in the art. Correction is necessary.

Claim 38 recites the phrase 'room temperature.' This phrase is indefinite in that the meets and bounds of the phrase are not clearly delineated. The phrase 'room temperature' is not a clear indication of a particular temperature. Because rooms vary in temperature ranges, it is suggested that the claim be rewritten to include an exact temperature or temperature range in place of 'room temperature' in order to further clarify the phrase. Clarification is necessary.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-10, 19-24 and 32-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for extracting the crude epicuticular layer of a plant via exposure to a solvent (and the corresponding crude product obtained therefrom), wherein said exposure does not cause damage to layers under the epidermal layer of the plant, does not reasonably provide enablement for an antiviral substance purified therefrom. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

Applicants have claimed a method for obtaining an antiviral preparation from a plant part, however, have not clearly disclosed which part of which plant actually provides for anti-viral

activity. Although it appears that Applicants have found an agent which possesses some *in-vitro* anti-viral activity, the agent has not been presented in such a way that the Skilled artisan would be able to reproduce such a method. For example, the *in-vitro* antiviral data as presented in the Examples beginning on page 13 of the Instant specification are not specific as to what part of the plant is being processed for an anti-viral product. Example 1, under 'Materials and Methods' states 'Samples were prepared by dipping intact plant parts...'. What parts is this sentence referring to? Applicants have stated in the Specification that different parts of the plant may be used, but have not provided any comparative evidence which would conclude that similar products will be obtained from say, an extraction on an apple seed -vs- an extraction on an apple leaf. With regard to active ingredients present in the cuticular layer, different parts of the plant; i.e., seed, could contain different defense agents (defensins) than another part of the plant (leaf). This is entirely possible because the respective parts of the plant are exposed to alternate environments; the seed is under the ground, defending from pests such as bacteria, while the stalk of the plant for example, may contain defensins to ward off insects.

Table 1 displays *in-vitro* anti-HSV results with regard to respective plant samples. However, only some of the numbers are represented by actual plants (as explained in the 'Results' section on p. 16). Thus, with regard to the other numbers which are not identified, it is left to the Skilled artisan to guess what plants these sample numbers correspond to. In the sentence before Table 1, it states that 'Samples extracted from...apple, avocado...tomato and cabbage hold

promise in this regard.' However, again, it remains unknown which part of the plants were actually used.

The Specification is not enabled for a protocol for the extraction of any plant/plant part to obtain an antiviral product. The state of the art is unpredictable. As evidenced by the data in the Instant specification, all of the samples which were assayed for anti-HSV activity had markedly different activities. For example, Sample # 61 displayed a TI of greater than 4.45%, while Sample #'s 57-59 displayed little or no activity. Thus, the method, as Instantly claimed is not enabled for every plant/plant part, as it is unpredictable, especially taking into consideration the myriad of plants which are known in the art to ascertain what, if any plants contain anti-viral substances within the cuticular layers.

Further, while the Specification has shown some positive result with regard to *in-vitro* HSV-1 and HIV-1 cytoprotection with an unknown part of willow, wax palm and plum, it is deemed that the Specification is not enabled for *in-vivo* efficacy. The efficacy of a drug treatment *in vivo* faces unfavorable obstacles not present in *in vitro* models. As such, *in vivo* utility necessarily involves unpredictability with respect to physiological activity of an asserted process in humans. See discussion in Ex parte Kranz, 19 USPQ 2d 1216, 1218-1219 (6/90). For examples, drug delivery to the target area must survive the acidic environment of the stomach if administered orally. Additionally, the delivery of the drug across necessary cell surfaces in

amounts needed to be efficacious, but not lethal to the subject, necessitates sensitive testing in order to adequately determine the proper human dosage.

To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve tedious trial and error protocols in order to ascertain exactly what plant part exhibited *in-vitro* antiviral activity.

Claims 25-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It appears, judging from the data set forth in the Disclosure, that Applicants have found a substance which provides for some *in-vitro* antiviral activity. However, it is not known what this substance is, or exactly how to obtain it. Thus, what the Applicants have disclosed is a method for extracting away the outer layers (epicuticular) of a plant. However, it is deemed that claims 25-31 which are drawn to specific viruses which may be treated with the product obtained from the epicuticular layer are not enabled because Applicants have not clearly taught how to make such a product via providing information regarding which plants/plant parts actually produce such

an antiviral substance (Please also see 112 First paragraph rejection under Scope of Enablement *supra* which apply to this Enablement rejection as well).

In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, *he must not be permitted to achieve this dominance by claims which are insufficiently supported* and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved." (emphasis added).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5-7, 10, 19-23, 32 and 36-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Lajide et al. (1996). Claims 5-7, 10, 19-23, 32 and 36-37 are drawn to a method for extracting the epicuticular layer away from the underlying layer of a plant or plant part (crude epicuticular product). Claims are further drawn to wherein the epicuticular layer is exposed to solvent via dipping, wherein the product obtained from solvent extraction is dissolved in a biologically compatible medium, wherein the crude product is further clarified, wherein the crude product is formulated into a pharmaceutical/nutraceutical composition, the plant or plant part is exposed to a solvent from about three minutes to about five minutes or a 'brief period of time,' and wherein the solvent comprises solutions such as hexane and chloroform for example. Claim 10 is drawn to a composition obtained via extraction of the epicuticular layer.

Lajide et al. (1996) studied bioactive constituents present in the epicuticular layers of 12 plants. Lajide et al. explained that plants excreted defensive phytochemicls into the epicuticular layers which may have had some pesticidal properties (p.259). Lajide et al.'s method for extracting away the waxy, epicuticular layer included dipping fresh leaves of each of the 12 plants (Please see 'Plant Materials' pp. 260) into chloroform for 3 minutes,

evaporating the chloroform via vacuum filtration, and precipitation with acetone with further evaporation (p. 260- 'Extraction Method'). The evaporated product was then brought up to volume with acetone, mixed with cellulose powder and reevaporated via desiccation and added to food (a biologically compatible medium - pharmaceutical/nutricutical composition) (p. 26- ' Diet incorporation bioassay').

Lajide et al. performed the same extraction as Instantly claimed, and thus, the Invention was known in the art.

Claims 5-9, 10, 19, 21, 24, 32, 33, 36, 37 and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Nordby et al. (1991). Claims 8-9, 24, 33 and 39 are drawn to wherein the plant is sprayed with the solvent, wherein the removal of the solvent includes evaporation via rotary evaporation for example, wherein the plant or plant part is selected from plants such as Citrus, wherein the plant or plant part is fruit peel and a product obtained from such an extraction.

Nordby et al. (1991) analyzed the epicutiular, waxy layer of grapefruit peels via several methods. One method included spraying the grapefruit skin (peel) with a solution of hexane and eventually clarifying the product obtained therefrom (p. 958 - 'Special Treatments'). Another protocol included placing the fruit into chloroform for 5 minutes,

collecting the extract/chloroform solution and the solvent was removed via rotoevaporation (p. 958- 'Wax Isolation and Analyses'). A portion of the evaporated product was further clarified via TLC (p. 959) and further analyzed via GLC.

The Examiner has given the term 'dipping' the broadest interpretation within reason, and has deemed that 'dipping would be analogous to 'exposing' or 'soaking' or 'placing' and thus, Nordby et al. anticipated claim 7.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5-10, 19-24 and 32-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lajide et al. (1996) or Nordby et al. (1991) . Claims 34-35 and 38 are drawn to wherein the plant part is Malus or Lycopersicon, and wherein the plant or plant part is exposed to a room temperature solvent.

The teachings of Lajide et al. (1996) and Nordby et al. (1991) were discussed *supra*.

Neither reference disclosed extraction of the epicuticular layers of Malus or Lycopersicon, or wherein the plant or plant parts were exposed to a room temperature solvent.

With regard to the solvent being at room temperature, both references disclosed exposing the plant parts/fruit to chloroform. It was known in the art that chloroform was routinely used at ambient temperatures, since chloroform had a low flash point and evaporated quickly at higher temperatures. Thus, although the references were not specific as to wherein the chloroform was used at room temperature, one of ordinary skill in the art would have been reasonably apprised that the chloroform which both references referred to was near ambient temperatures ('room temperature'). Alternatively, one of ordinary skill in the art would have been apprised that lowering the temperature, and allowing the extraction to stand for a long period of time, 2 hours for example, would have been an **analogous reaction** which would have yielded similar if not exact extraction yields (The Arrhenious Principal). Thus, the ordinary artisan would have further known that the use of chloroform at lower temperatures would have produced the same outcome as compared to extraction with chloroform at an ambient temperature, although the extraction with colder chloroform would have taken a longer amount of time.

Although the references were silent with regard to other plant genus such as Malus, one of ordinary skill in the art would have been appraised of how to extract the epicuticular layers from these plants in view of Lajide et al. (1996) or Nordby et al. (1991). Relying on

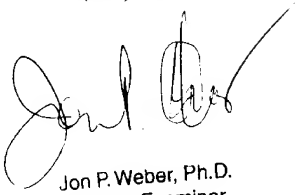
the references before him, the ordinary artisan would have a reasonable expectation that the addition of chloroform or hexane to the outer layer of the plant/plant part would dissolve the cuticular layer of the plant/plant part. One of ordinary skill in the art would be motivated to remove the cuticular layers from plants such as Malus in order to study the defensins intrinsic to the waxy layer of the plant in order to produce 'natural' plant insecticides.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Patricia Patten, whose telephone number is (703)308-1189. The examiner can normally be reached on M-F from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Jon P. Weber, Ph.D.
Primary Examiner